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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/725,276	12/02/2003	Jon Elliot Adler	T1530-00119	1816

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EXAMINER	
BRANNOCK, MICHAEL T	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 10/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/725,276	ADLER ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *235-286* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *235-286* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 May 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *none*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application: Claims and Amendments

Applicant is notified that the amendments put forth on 11/01/2005, have been entered in full. Claims 235-286 are pending and under examination in this Office Action.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, see page 16 for example. Applicant is required to delete the embedded hyperlinks and/or other form of browser-executable code. See MPEP 608.01. Furthermore, there is a blank at page 10. Appropriate correction is required

Claim Objections

Claim 235 is objected to because of the following informalities: the phrase "based its" in claim 235ii appears to be missing the word "on", i.e. "based on its".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 235-286 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 235, and dependent claims require a compound that "putatively" modulates or elicits human T1R2-associatied taste. It is unclear what limitations Applicant intends the world

putatively to add to the claims, and nor is such explained in the specification. Thus, an artisan could not be sure whether he or she was practicing or infringing on Applicant's claims.

Claims 235 and 244 require that the nucleic acid hybridize under stringent conditions. The term stringent conditions is a relative term and encompasses conditions of varying degrees of stringency - such conditions determining the bounds of the claim. However, the art does not provide an unambiguous definition of the term "stringent conditions" and neither is such a definition given for the term in the specification which puts forth the metes and bounds of the claim Applicant is seeking protection for. The term appears to be defined only by way of example at page 30. It is suggested that the claim recite the actual conditions that applicant considers to be stringent, e.g., salt concentration and temperature conditions of incubations and washes.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 235 and 243-286 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for assay methods employing polypeptides that are at least 90% identical to SEQ ID NO: 20 and are encoded by polynucleotides that hybridize to a polynucleotide of SEQ ID NO: 20 under the stringent conditions set forth in lines 16-20 of page 30 of the specification and encode a polypeptide that bind sucrose in conjunction with a T1R3 polypeptide, does not reasonably provide enablement for methods employing the vast genus of structurally divergent polypeptides encompassed by the claims or for fragments of the T1R2

polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims encompass vast genus of structurally divergent polypeptides, e.g. those that comprise polynucleotides encoding polypeptide variants of the polypeptide of SEQ ID NO: 21, i.e. substitutions, deletions or insertions in a protein corresponding to SEQ ID NO: 21. Applicant has not provided sufficient guidance as to how to make and use the encoded polypeptides or fragments in the claimed methods. The specification has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make or which fragments provide the required functional activity. If a variant of the protein corresponding to SEQ ID NO: 21 is to have a structure and function similar to the protein corresponding to SEQ ID NO: 21 then the specification has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make that will preserve the structure and function of the protein corresponding to SEQ ID NO: 21. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions (see Bowie et al., 1990, Science

247:1306-1310, especially p.1306, column 2, paragraph 2). Guo-HH et al. PNAS 101(25)9205-9210, 2004, recently reviewed the art and conducted an extensive study on the effect of amino acid substitution on the functionality of a wide variety of proteins and found that on average a single amino acid substitution had a 34% chance inactivating the functionality of the protein, see the Abstract. However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Also, these or other regions may be critical determinants of antigenicity. It is well appreciated in the art of antibody production that it is unpredictable which amino acids are critical antigenic determinants (see Alexander et al., Proc. Natl. Acad. Sci. 89(3352-3356)1992. Protein antigenicity can be significantly reduced by substitution of even a single residue. Further, even if an amino acid substitution does not destroy the activity of the immunizing protein, the substitution may significantly reduce the antigenicity of the protein (see the Abstract of Alexander et al.). The specification does not provide sufficient guidance as to how to make antibodies that are specific to variants of SEQ ID NO: 21 that can be used for any specific purpose. The specification has not provided guidance as to natural variants that may exist, nor how to use antibodies specific to variants that might be created.

Although the specification outlines art-recognized procedures for producing variants, this is not adequate guidance as to the nature of active variants that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may

not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity.

The problem of producing active variants appears especially difficult in the art of T1R receptors, to which the instant polypeptide is asserted to belong. The instant specification appears to simply suggest to the artisan that art-recognized procedures for screening GPCRs (e.g. pages 32-33, 40 and the example at page 91) are sufficient to identify functional variants of SEQ ID NO: 21. However, Hoon *et al., Cell* 96(541-551)1999, report that "We have attempted to determine the ligand/tastant specificity of TR1 and TR2 using a variety of strategies but have been hampered by the difficulty of functionally expressing these molecules in heterologous systems" see col 1 of page 547. The art regarding T1R receptors, as exemplified by Hoon et al., recognizes the complexity, unpredictability, and non-routine nature of the work involved in trying to assay functional T1R receptors. While, it may be reasonable that the instant specification is enabling for variants that are at least 90% identical to SEQ ID NO: 21, see copending Application 09799629, the scope of the instant claims is vastly wider than such and does not appear to be supported by and adequate disclosure.

Due to the large quantity of experimentation necessary to generate the infinite number of variants recited in the claims and screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes

the unpredictability of the and the difficulties encountered in screening T1Rs, exemplifed by Hoon et al. and the breadth of the claims which fail to recite sufficient structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 235 and 243-286 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses a naturally occurring polynucleotide of SEQ ID NO: 20 encoding a polypeptide of SEQ ID NO: 21, yet the claims encompass methods requiring polypeptide fragments or polypeptides encoded by polynucleotides that need only hybridize to fragments of a polynucleotide of SEQ ID NO: 20. These claimed genera do not meet the written description provision of 35 U.S.C. 112, first paragraph. Although one of skill in the art would reasonably predict that these sequences exist or could be made to exist and be useful in the claimed methods, one would not be able make useful predictions as to the amino positions or identities of those sequences based on the information disclosed in the specification.

A genus claim may be supported by a representative number of species as set forth in Regents of the University of California v Eli Lilly & Co, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which

features constitute a substantial portion of the genus. The instant specification discloses no artificially mutated sequences that have any function. Further, even if the disclose sequence were definitive of a genus with a specified function, the instantly claimed genus is not so limited and the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify/obtain the polypeptides encompassed, thus the artisan would not consider Applicant to be in possession of the breadth that is claimed.

With the exception of the polypeptide of SEQ ID NO: 21, and polypeptides at least 90% identical to SEQ ID NO: 21, see copending Application 09799629, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of variants, therefore the full breadth of the claims do not meet the written description provision of 35 U.S.C. §112, first paragraph.

Conclusion

No claim is allowable.

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1649.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D., can be reached at (571) 272-0867. Official papers filed by fax should be directed to **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

October 2, 2006

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER